ISPH-0782 - 114 - PATENT

## What is claimed is:

- 1. An antisense compound 8 to 30 nucleobases in length which modulates interleukin-5 signal transduction.
- 2. The antisense compound of claim 1 which is an 5 antisense oligonucleotide.
  - 3. The antisense compound of claim 1 which is targeted to a nucleic acid molecule encoding mammalian interleukin-5, wherein said antisense compound modulates the expression of mammalian interleukin-5.

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- 4. An antisense compound up to 30 nucleobases in length comprising at least an 8-nucleobase portion of SEQ ID NO: 52, 53 or 62 which inhibits the expression of mammalian interleukin-5.
- 5. The antisense compound of claim 1 which is targeted to a nucleic acid molecule encoding a mammalian interleukin-5 receptor a, wherein said antisense compound modulates the expression of mammalian interleukin-5 receptor a.
- 6. An antisense compound up to 30 nucleobases in length comprising at least an 8-nucleobase portion of SEQ ID NO: 162, 166, 167, 169, 170, 171 or 172 which inhibits the expression of mammalian interleukin-5 receptor a.
- 7. The antisense compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage.
  - 8. The antisense compound of claim 7 wherein the modified internucleoside linkage of the antisense oligonucleotide is a phosphorothicate linkage.

- 9. The antisense compound of claim 7 wherein the modified internucleoside linkage of the antisense oligonucleotide is a peptide nucleic acid.
- 10. The antisense compound of claim 9 which comprises 5 at least one basic amino acid conjugated to at least one end of the antisense compound.
  - 11. The antisense compound of claim 10 wherein the basic amino acid is lysine or arginine.
- 12. The antisense compound of claim 10 which is less 10 than 20 nucleobases in length.
  - 13. The antisense compound of claim 12 comprising at least an 8-nucleobase portion of SEQ. ID NO: 209.
- 14. The antisense compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified sugar moiety.
  - 15. The antisense compound of claim 14 wherein the modified sugar moiety of the antisense oligonucleotide is a 2'-O-methoxyethyl sugar moiety.
- 16. The antisense compound of claim 15 wherein 20 substantially all sugar moieties of the antisense oligonucleotide are 2'-O-methoxyethyl sugar moieties.
  - 17. The antisense compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified nucleobase.

- 18. The antisense compound of claim 17 wherein the modified nucleobase of the antisense oligonucleotide is a 5- methylcytosine.
- 19. The antisense compound of claim 15 wherein each 2'5 O-methoxyethyl modified cytosine nucleobase of the antisense oligonucleotide is a 5-methylcytosine.
  - 20. The antisense compound of claim 1 which is a chimeric oligonucleotide.
- 21. A pharmaceutical composition comprising the 10 antisense compound of claim 1 and a pharmaceutically acceptable carrier or diluent.
  - 22. The pharmaceutical composition of claim 21 further comprising a colloidal dispersion system.
- 15 23. The pharmaceutical composition of claim 21 wherein the antisense compound is an antisense oligonucleotide.
  - 24. The antisense compound of claim 5 which is targeted to soluble interleukin-5 receptor a and which preferentially inhibits the expression of soluble interleukin-5 receptor a.
- 25. The antisense compound of claim 24 which is targeted to a region of a nucleic acid molecule encoding soluble interleukin-5 receptor a which is not found in a nucleic acid molecule encoding membrane interleukin-5 receptor a.
- 26. The antisense compound of claim 5 which is targeted to membrane interleukin-5 receptor a and which preferentially inhibits the expression of membrane interleukin-5 receptor a.

- 27. The antisense compound of claim 26 which is targeted to a region of a nucleic acid molecule encoding membrane interleukin-5 receptor a which is not found in a nucleic acid molecule encoding soluble interleukin-5 receptor 5 a.
  - 28. The antisense compound of claim 5 which inhibits the expression of both soluble and membrane forms of interleukin-5 receptor a.
- 29. The antisense compound of claim 5 which alters the 10 ratio of interleukin-5 receptor a isoforms expressed by a cell or tissue.
- 30. The antisense compound of claim 29 which increases the ratio of the soluble form of interleukin-5 receptor a to the membrane form of interleukin-5 receptor a expressed.
  - 31. The antisense compound of claim 30 which is an antisense oligonucleotide wherein substantially all sugar moieties of the antisense oligonucleotide are 2'-O-methoxyethyl sugar moieties.
- 32. The antisense compound of claim 5 which promotes apoptosis.
- 33. An antisense compound which alters splicing of an RNA encoding interleukin-5 receptor a, such that the ratio of interleukin-5 receptor a isoforms is altered.
  - 34. The antisense compound of claim 33 wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage.

- 35. The antisense compound of claim 34 wherein the modified internucleoside linkage of the antisense oligonucleotide is a phosphorothioate linkage.
- 36. The antisense compound of claim 34 wherein the 5 modified internucleoside linkage is a peptide nucleic acid.
  - 37. The antisense compound of claim 36 which comprises at least one basic amino acid conjugated to at least one end of the antisense compound.
- 38. The antisense compound of claim 37 wherein the 10 basic amino acid is lysine or arginine.
  - 39. The antisense compound of claim 38 which is less than 20 nucleobases in length.
  - 40. The antisense compound of claim 36 comprising at least an 8-nucleobase portion of SEQ. ID NO: 209.
- 15 41. The antisense compound of claim 33 wherein the antisense oligonucleotide comprises at least one modified sugar moiety.
- 42. The antisense compound of claim 41 wherein the modified sugar moiety of the antisense oligonucleotide is a 2'-O-methoxyethyl sugar moiety.
- 43. The antisense compound of claim 42 wherein substantially all sugar moieties of the antisense oligonucleotide are 2'-O-methoxyethyl sugar moieties.
  - 44. The antisense compound of claim 33 wherein the antisense oligonucleotide comprises at least one modified nucleobase.

- 45. The antisense compound of claim 44 wherein the modified nucleobase of the antisense oligonucleotide is a 5-methylcytosine.
- 46. The antisense compound of claim 42 wherein each 2'5 O-methoxyethyl modified cytosine nucleobase of the antisense oligonucleotide is a 5-methylcytosine.
- 47. The antisense compound of claim 33 which comprises a conjugate group of at least one lysine or arginine linked to the antisense compound.
  - 48. The antisense compound of claim 33 which is a chimeric oligonucleotide.
- 49. A method of modulating interleukin-5 signal transduction in cells or tissues comprising contacting said cells or tissues with the antisense compound of claim 1 so that interleukin-5 signal transduction is modulated.
- 50. A method of modulating the expression of mammalian interleukin-5 in mammalian cells or tissues comprising contacting said cells or tissues with the antisense compound of claim 3 so that expression of mammalian interleukin-5 is inhibited.
- 51. A method of modulating the expression of mammalian interleukin-5 receptor a in mammalian cells or tissues comprising contacting said cells or tissues with the antisense compound of claim 33 so that expression of mammalian interleukin-5 receptor a is inhibited.

- 52. A method of altering the ratio of the isoforms of mammalian interleukin-5 receptor a in mammalian cells or tissues comprising contacting said cells or tissues with the antisense compound of claim 33 so that the ratio of the mammalian interleukin-5 receptor a isoforms is altered.
- 53. A method of modulating the expression of mammalian interleukin-5 receptor a in mammalia cells or tissues comprising contacting said cells or tissues with the antisense compound of claim 5 so that expression of mammalian interleukin-5 receptor a is inhibited.
- 54. A method of altering the ratio of the isoforms of mammalian interleukin-5 receptor a in mammalian cells or tissues comprising contacting said cells or tissues with the antisense compound of claim 31 so that the ratio of the mammalian interleukin-5 receptor a isoforms is altered.
- 55. A method of treating a mammalian having a disease or condition associated with interleukin-5 signal transduction comprising administering to said mammal a therapeutically or prophylactically effective amount of the antisense compound of claim 1 so that interleukin-5 signal transduction is modulated.
- 56. A method of treating a mammal having a disease or condition associated with interleukin-5 expression comprising administering to said mammal a therapeutically or prophylactically effective amount of the antisense compound of claim 3 so that interleukin-5 expression is modulated.
- 57. A method of treating a mammal having a disease or condition associated with interleukin-5 receptor a expression comprising administering to said mammal a therapeutically or prophylactically effective amount of the antisense compound

of claim 5 so that interleukin-5 receptor a expression is modulated.

- 58. The method of claim 57 wherein the disease or condition is an eosinophilic syndrome or asthma.
- 5 59. The method of claim 57 wherein the route of administration is pulmonary administration.
- 60. A method of treating a mammal having a disease or condition associated with interleukin-5 receptor a expression comprising administering to said mammal a therapeutically or prophylactically effective amount of the antisense compound of claim 33 so that the ratio of interleukin-5 receptor a isoforms is altered.
- 61. The method of claim 60 wherein the disease or condition is an eosinophilic syndrome or asthma.
  - 62. The method of claim 60 wherein the route of administration is pulmonary administration.
- 63. A method of treating a mammal having a disease or condition characterized by a reduction in apoptosis comprising administering to said mammal a prophylactically or therapeutically effective amount of the antisense compound of claim 32.
- 64. A method of treating a mammal having a disease or condition associated with interleukin-5 receptor a expression comprising administering to said mammal a therapeutically or prophylactically effective amount of the antisense compound of claim 26 so that expression of membrane interleukin-5 receptor a is modulated.

- 65. The method of claim 64 wherein the disease or condition is asthma or an eosinophilic syndrome.
- 66. The method of claim 64 wherein the route of administration is pulmonary administration.
- 67. The pharmaceutical composition of claim 21 further comprising a chemotherapeutic agent for the treatment of asthma.
- 68. A pharmaceutical composition comprising the antisense compound of claim 28 and a pharmaceutically acceptable carrier or diluent.
  - 69. A pharmaceutical composition comprising the antisense compound of claim 36 and a pharmaceutically acceptable carrier or diluent.
- 70. A diagnostic kit for detecting the expression level of the membrane versus soluble form of IL-5 Receptor a.
  - 71. The diagnostic kit of claim 70 comprising the antisense compound of claim 33.
- 72. The diagnostic kit of claim 71 wherein the 20 antisense compound is a peptide nucleic acid.